

Amendments to the Claims:

Claims 1-45 (Cancelled)

46. (Currently amended) An isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:5, wherein said polypeptide does not bind to choline ~~and has lectin~~ activity.

47. (Previously presented) The isolated polypeptide of claim 46, wherein said polypeptide comprises SEQ ID NO:3.

48. (Previously presented) The isolated polypeptide of claim 46, wherein said polypeptide comprises SEQ ID NO:1.

49. (Previously presented) The isolated polypeptide of claim 46, wherein said polypeptide comprises SEQ ID NO:24.

50. (Previously presented) The isolated polypeptide of claim 46, wherein said polypeptide is immunogenic.

51. (Previously presented) The isolated polypeptide of claim 46, wherein said polypeptide comprises an amino acid sequence having up to 475 amino acids.

52. (Previously presented) The isolated polypeptide of claim 51, wherein said polypeptide comprises an amino acid sequence having up to 460 amino acids.

53. (Withdrawn) A pharmaceutical composition comprising the polypeptide of claim 46 and a pharmaceutically acceptable ~~adjuvant~~, carrier, or diluent.

54. (Currently amended) An isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:4, wherein said polypeptide does not bind to choline ~~and has lectin activity~~.

55. (Previously presented) The isolated polypeptide of claim 54, wherein said polypeptide comprises SEQ ID NO:22.

56. (Previously presented) The isolated polypeptide of claim 54, wherein said polypeptide is immunogenic.

57. (Previously presented) The isolated polypeptide of claim 54, wherein said polypeptide comprises an amino acid sequence having up to 475 amino acids.

58. (Previously presented) The isolated polypeptide of claim 54, wherein said polypeptide comprises an amino acid sequence having up to 460 amino acids.

59. (Currently amended) An isolated polypeptide comprising a fragment of ~~an~~ the amino acid sequence of SEQ ID NO:24, wherein said fragment does not bind to choline, ~~has lectin activity~~ and comprises at least 138 consecutive amino acids of SEQ ID NO:24, wherein said polypeptide is immunogenic.

60. (Currently amended) An isolated polypeptide comprising ~~an~~ the amino acid sequence as set forth in SEQ ID NO:5, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic and said polypeptide comprises up to 398 amino acids.

61. (Currently amended) An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:3, wherein said amino acid sequence comprises at least one to

57 amino acid substitutions, and said polypeptide does not bind choline and ~~has lectin activity~~ wherein said polypeptide is immunogenic.

62. (Currently amended) The isolated polypeptide of claim 61, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:1, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline and ~~has lectin activity~~ wherein said polypeptide is immunogenic.

63. (Currently amended) The isolated polypeptide of claim 61, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:24, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline and ~~has lectin activity~~ wherein said polypeptide is immunogenic.

64. (Cancelled)

65. (Cancelled)

66. (Previously presented) The isolated polypeptide of claim 60, wherein said amino acid substitutions comprise conservative amino acid substitutions.

67. (Currently amended) An isolated polypeptide comprising ~~an~~ the amino acid sequence set forth in SEQ ID NO:4, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, wherein said polypeptide does not bind choline and ~~has lectin activity~~ wherein said polypeptide is immunogenic and said polypeptide comprises up to 398 amino acids.

68. (Currently amended) The isolated polypeptide of claim 67, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:22, wherein said amino

acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline and ~~has lectin activity~~ wherein said polypeptide is immunogenic.

69. (Currently amended) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) an analog of the amino acid sequence set forth in SEQ ID NO:5, wherein said polypeptide does not bind choline and ~~has lectin activity~~ is immunogenic;
- b) an analog of the amino acid sequence set forth in SEQ ID NO:4, wherein said polypeptide does not bind choline and ~~has lectin activity~~ is immunogenic;
- c) an analog of the amino acid sequence set forth in SEQ ID NO:11, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic, and comprise up to 328 amino acids;
- d) an analog of the amino acid sequence set forth in SEQ ID NO:9, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic, and comprises up to 376 amino acids; and,
- e) an analog of the amino acid sequence set forth in SEQ ID NO:10, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic and comprises up to 328 amino acids.

70. (Currently amended) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) a derivative of the amino acid sequence set forth in SEQ ID NO:5, wherein said polypeptide does not bind choline and ~~has lectin activity~~ is immunogenic;
- b) a derivative of the amino acid sequence set forth in SEQ ID NO:4, wherein said polypeptide does not bind choline and ~~has lectin activity~~ is immunogenic;
- c) a derivative of the amino acid sequence set forth in SEQ ID NO:11, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic, and comprise up to 328 amino acids;

d) a derivative of the amino acid sequence set forth in SEQ ID NO:9, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic, and comprises up to 376 amino acids; and,

e) a derivative of the amino acid sequence set forth in SEQ ID NO:10, wherein said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic and comprises up to 328 amino acids.

71. (Currently amended) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence set forth in SEQ ID NO:5 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide comprises up to 398 amino acids, ~~retains native tertiary structure~~, does not bind choline and ~~has lectin activity~~ is immunogenic, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide;

b) the amino acid sequence set forth in SEQ ID NO:4 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide comprises up to 398 amino acids, ~~retains native tertiary structure~~, does not bind choline and ~~has lectin activity~~ is immunogenic, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide;

c) the amino acid sequence set forth in SEQ ID NO:11 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide ~~retains native tertiary structure~~, does not bind choline and ~~has lectin activity~~ is immunogenic, and comprise up to 328 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide;

d) the amino acid sequence set forth in SEQ ID NO:9 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide ~~retains native tertiary structure~~, does not bind choline and ~~has lectin activity~~ is immunogenic, and comprises up to 376 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide;

e) the amino acid sequence set forth in SEQ ID NO:10 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide ~~retains native tertiary structure~~, does not bind choline, ~~and has lectin activity~~ is immunogenic and comprises up to 328 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide; and,

f) the amino acid sequence set forth in SEQ ID NO:3 wherein said amino acid sequence comprises at least one to 57 amino acid substitutions and said polypeptide ~~retains native tertiary structure~~, does not bind choline and ~~has lectin activity~~ is immunogenic, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide.

72. (Currently amended) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence set forth in SEQ ID NO:5, wherein said polypeptide ~~retains native tertiary structure~~, does not bind choline, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide ~~and has lectin activity~~;

b) the amino acid sequence set forth in SEQ ID NO:4, wherein said polypeptide ~~retains native tertiary structure~~, does not bind choline, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CpbA polypeptide ~~and has lectin activity~~;

c) the amino acid sequence set forth in SEQ ID NO:11, wherein said polypeptide ~~retains native tertiary structure~~, does not bind choline ~~and has lectin activity~~, is immunogenic and comprise up to 328 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide;

d) the amino acid sequence set forth in SEQ ID NO:9, wherein said polypeptide ~~retains native tertiary structure~~, does not bind choline ~~and has lectin activity~~, is immunogenic and comprises up to 376 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with the full-length CbpA polypeptide; and,

e) the amino acid sequence set forth in SEQ ID NO:10, wherein said polypeptide ~~retains native tertiary structure,~~ does not bind choline ~~and has lectin activity,~~ is immunogenic and comprises up to 328 amino acids, wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide.

73. (Cancelled)

74. (Currently amended) An isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:11, wherein said polypeptide does not bind to choline ~~and has lectin activity,~~ and comprises up to 328 amino acids.

75. (Currently amended) An isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:9, wherein said polypeptide does not bind to choline ~~and has lectin activity,~~ and comprises up to 376 amino acids.

76. (Previously presented) The isolated polypeptide of claim 75, wherein said polypeptide comprises SEQ ID NO:7.

77. (Previously presented) The isolated polypeptide of claim 74, wherein said polypeptide is immunogenic.

78. (Previously presented) The isolated polypeptide of claim 75, wherein said polypeptide is immunogenic.

79. (Cancelled)

80. (Withdrawn) A pharmaceutical composition comprising the polypeptide of claim 74 and a pharmaceutically acceptable ~~adjuvant,~~ carrier, or diluent.

81. (Currently amended) An isolated polypeptide comprising an amino acid sequence as set forth in SEQ ID NO:10, wherein said polypeptide does not bind to choline; and ~~has-lectin activity~~ said polypeptide comprises up to 328 amino acids.

82. (Previously presented) The isolated polypeptide of claim 81, wherein said polypeptide comprises SEQ ID NO:23.

83. (Previously presented) The isolated polypeptide of claim 81, wherein said polypeptide is immunogenic.

Claims 84-86 (Cancelled)

87. (Currently amended) An isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO:11, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline ~~and has-lectin activity~~, is immunogenic and comprises up to 328 amino acids.

88. (Currently amended) The isolated polypeptide of claim 87, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:9, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline and ~~has-lectin activity~~ is immunogenic.

89. (Currently amended) The isolated polypeptide of claim 87, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:7, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline and ~~has-lectin activity~~ is immunogenic.

90. (Cancelled)

91. (Cancelled)

92. (Previously presented) The isolated polypeptide of claim 87, wherein said amino acid substitutions comprise conservative amino acid substitutions.

93. (Currently amended) An isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO:10, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline, ~~and has lectin activity~~ is immunogenic and comprises up to 328 amino acids.

94. (Currently amended) The isolated polypeptide of claim 93, wherein said polypeptide comprises the amino acid sequence set forth in SEQ ID NO:23, wherein said amino acid sequence comprises at least one to 57 amino acid substitutions, and said polypeptide does not bind choline ~~and has lectin activity~~ is immunogenic.

95. (Withdrawn) A pharmaceutical composition comprising the polypeptide of claim 75 and a pharmaceutically acceptable ~~adjuvant~~, carrier, or diluent.

96. (Cancelled)

97. (Cancelled)

98. (Previously presented) The isolated polypeptide of claim 61, wherein said amino acid substitutions comprise conservative amino acid substitutions.

Claims 99-110 (Not entered)

111. (New) The isolated polypeptide of claim 59, wherein said polypeptide has lectin activity.

112. (New) The isolated polypeptide of claim 60, wherein said polypeptide has lectin activity.

113. (New) The isolated polypeptide of claim 61, wherein said polypeptide has lectin activity.

114. (New) The isolated polypeptide of claim 62, wherein said polypeptide has lectin activity.

115. (New) The isolated polypeptide of claim 63, wherein said polypeptide has lectin activity.

116. (New) The isolated polypeptide of claim 67, wherein said polypeptide has lectin activity.

117. (New) The isolated polypeptide of claim 68, wherein said polypeptide has lectin activity.

118. (New) The isolated polypeptide of claim 87, wherein said polypeptide has lectin activity.

119. (New) The isolated polypeptide of claim 88, wherein said polypeptide has lectin activity.

120. (New) The isolated polypeptide of claim 89, wherein said polypeptide has lectin activity.

121. (New) The isolated polypeptide of claim 93, wherein said polypeptide has lectin activity.

122. (New) The isolated polypeptide of claim 94, wherein said polypeptide has lectin activity.

REMARKS/ARGUMENTS

Status of the Claims

Claims 1-45, 64, 65, 73, 79, 84-86, 90, 91, 96 and 97 have been canceled without prejudice to or disclaimer of the subject matter therein. Applicants' reserve the right to file a continuation or divisional application directed to the subject matter canceled during prosecution of this application.

Claims 111-122 have been added.

Claims 46-63, 66-72, 74-78, 80-83, 87-89, 92-95, 98 and 111-122 are now pending.

The Examiner's comments are addressed below in the order set forth in the Office Action.

Amendments to the Claims

Claims 46, 53, 54, 59-63, 67-72, 74-75, 80, 81, 87-89, and 93-95 have been amended as described below. Support for these amendments is found throughout the specification and in the originally filed claims. Therefore, no new matter has been added by way of claim amendment.

Specifically, claims 46, 54, 59-63, 67-72, 74-75, 81, 87-89, and 93-94 have been amended to no longer recite "has lectin activity". Support for this amendment can be found, for example, in the claims as originally filed. In addition, claims 59-63, 67-72, 87-89, and 93-94, have been amended to recite that the polypeptide is "immunogenic." Support for this amendment can be found throughout the specification, for example, on page 3, lines 23-25.

Claims 53, 80, and 96 have been amended to remove the term "adjuvant". Support for this amendment can be found, for example, in original claim 39.

Claims 71 and 72 have been amended to recite the polypeptide "interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide." Support for this amendment can be found, for example, on pages 64, 65, page 33, lines 29-33, and pages 34 and 35.

Claims 111-122 have been added and recite "lectin activity." Support for this amendment can be found throughout the specification. See, for example, page 20, lines 18-25 and in Example 2.

No new matter has been added by way of these amendments.

Election/Restriction

I. The Examiner concludes claims 64, 90, and 95 are directed to a polypeptide that is "immunogenic against bacterial infection" and therefore are drawn to a non-elected invention. Applicants note claim 95 does not have this limitation and assume the rejection was intended to be applied to claim 96. Claims 64, 90, and 96 have been canceled without prejudice or disclaimer due to Restriction.

II. The Examiner further concludes claims 53, 80, and 96, which are drawn to pharmaceutical compositions, are directed to non-elected inventions. Applicants note claim 96 does not have this limitation and assume the rejection was intended to be applied to claim 95. Applicants respectfully traverse.

Claims 53, 80, and 95 have been amended to remove the term "adjuvant". Support for this amendment can be found, for example, on page 43, lines 23-25 of the specification and in original claim 39. Originally filed claim 39 recited a "pharmaceutical composition comprising an amount of the polypeptide of claim 1 and a pharmaceutically acceptable carrier or diluent." The Restriction Requirement (mailed August 18, 1999) classified original claim 39 into Group I. Group I further encompassed original claims 1-18 and was characterized as "drawn to polypeptides, classified in class 530, subclass 350." Accordingly, per the Restriction Requirement of August 18, 1999, claims 53, 80, and 95, as amended, are drawn to the elected invention and the Examiner is respectfully requested to reconsider the Restriction and exam claims 53, 80, and 95 in the instant application. Alternatively, the Examiner is requested to issue a new Restriction Requirement in the present case.

III. The Office Action further states that the broadest reasonable interpretation of "immunogenic" includes the ability to raise an antibody against the recited polypeptide. The Office Action continues that "claims reciting 'polypeptide is immunogenic' are not considered to be directed to vaccines" (Final Office Action, mailed March 6, 2003, page 3). Applicants clarify

that a polypeptide that is "immunogenic" has many recognized uses, one of which includes the use as a vaccine.

The Rejection of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

"New Matter" under 35 U.S.C. §112, First Paragraph

Claims 51, 57-63, 65-68, 71-72, 79, 84-89, and 91-94 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner has stated that this is a "new matter" rejection. This rejection is respectfully traversed.

I. The Examiner continues to maintain that claims 51 and 57, which recite "up to 475 amino acids" contain new matter. This rejection is respectfully traversed.

Claim 51 and claim 57 recite a polypeptide having the amino acid sequence of SEQ ID NO: 5 and 6, wherein said polypeptide does not bind choline and comprises up to "475 amino acids" in length.

First, the Examiner states "Applicants appear to believe the claim encompasses *fragments* of these disclosed proteins that include the named subsequences in the recited SEQ ID NO" (emphasis added, Final Office Action mailed March 6, 2003, page 4, paragraph 2). Based on this understanding of the claim, the Examiner concludes that 1) the subgenus of "*fragments*" is not contemplated by the specification; and, 2) the claims are not limited to the concept.

Contrary to the assumption made in the Office Action, claims 51 and 57 do not encompass *fragments* of SEQ ID NO: 5 and 4. See, page 14, lines 9-10 of the Amendment and Response mailed December 12, 2002 which states "[d]ependent claims 51, 57, 78, and 84 cannot be broader than their respective independent claims and therefore also *do not encompass fragments*" (emphasis added). The Examiner correctly articulates on page 4, paragraph 2, lines 6-8 of the Final Office Action (mailed March 6, 2003) that claims 51 and 57 "embrace any

protein of the recited size (i.e., up to 475 amino acids) having the recited sequence (i.e. SEQ ID NO:5) embedded in it".

The "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." *In re Edwards*, 196 USPQ 465 (CCPA 1979). Applicants maintain that the reasons made of record in the Amendment and Response filed on December 12, 2002 provide ample guidance to one of skill in the art that the inventors had possession of the claimed invention at the time of filing and therefore do not constitute "new matter" as asserted in the Office Action.

Briefly, as acknowledged by the Examiner, page 7, lines 3-5 of the specification discloses a 475 amino acid N-terminal choline binding protein A truncate. In addition, page 6, lines 5-6 of the specification indicates that the invention provides an isolated polypeptide "*comprising* an amino acid sequence of an N-terminal choline binding protein" and further provides specific SEQ ID NOs containing such sequences. Moreover, page 13, lines 5-10 of the specification indicates that polypeptides of the invention may be changed or modified "wherein one or more residues are added to a terminal portion". Accordingly, no new matter has been added in these claims.

To further illustrate this point, claims 46 and 51 are reproduced below:

Claim 46. An isolated polypeptide *comprising* an amino acid sequence as set forth in SEQ ID NO:5, wherein said polypeptide does not bind to choline and is immunogenic.

Claim 51. The isolated polypeptide of claim 46, wherein said polypeptide comprises an amino acid sequence having up to 475 amino acids.

Claim 46 employs open language and therefore encompasses polypeptides with any additional amino acid sequence at either terminal of SEQ ID NO:5. Given the Examiner's acknowledgment that claim 46 has satisfied 35 U.S.C. §112, first paragraph; the literal support for a peptide of 475 amino acids that appears on page 7, lines 1-6 of the specification; and, the

explicit recitation that one or more residues can be added to the terminal portion of a sequence of the invention, it is clear that claim 51, which merely limits the maximum number of amino acids for the polypeptide of claim 46 does not constitute "new matter." Thus, the "new matter" rejection under 35 U.S.C. §112, first paragraph, should be withdrawn. This same rationale applies to claim 57. The Examiner is respectfully requested to withdraw the rejection of claims 51 and 57 under 35 U.S.C. §112, first paragraph.

The Examiner is reminded, that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Applicant submits that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a sequence having the amino acid sequence of SEQ ID NO:5 or 4 having up to 475 amino acids.

The "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" (66 Fed. Reg. 1099, 1106 (2000)) state that genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics, *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993).

The structural limitations recited in claims 51 and 57 meet this requirement. The recitation of a sequence comprising the amino acid sequence of SEQ ID NO:5 and 4 and comprising up to 475 amino acids is a *very predictable structure* of the sequences encompassed by the claimed invention. This structural limitation is sufficient to distinguish the claimed

nucleotide sequences from other materials and thus sufficiently identifies the structural characteristics that define the claimed genus. Moreover, the specification provides three representative species of the genus of claim 51 (i.e., SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:24) and three representative species of the genus of claim 57 (i.e., SEQ ID NO: 1, SEQ ID NO: 22, and SEQ ID NO: 24). (see Appendix A attached herewith)

Furthermore, the court in *Lilly* held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus *or* of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." 119 F.3d at 1569, *emphasis added*. The recitation of a predictable structure of an amino acid sequence of SEQ ID NO:5 having up to 475 amino acids is sufficient to satisfy the written description requirement. Accordingly, this limitation satisfies the written description standard set forth in *Lilly*. Claims 51 and 57 satisfy the written description requirement under 35 U.S.C. §112, first paragraph and the Examiner is respectfully requested to withdraw the rejection.

It is further noted that "the Examiner (or the Board, if the Board is the first body to raise a particular ground for rejection) 'bears the initial burden . . . of presenting a *prima facie* case of unpatentability' . . . Insofar as the written description requirement is concerned, that burden is discharged by 'presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.'" *In re Alton*, 37 USPQ 2d at 1583-84 (Fed. Cir. 1996). As the Examiner's explanation as to why the claims 51 and 57 constitute new matter were made based on an incorrect interpretation of the claims, if the rejection is maintained, a further explanation of the rejection is respectfully requested.

II. The Examiner maintains that claims 52 and 58, which recite "up to 460 amino acids," contain "new matter." This rejection is respectfully traversed.

The Office Action applies the same reasoning for the new matter rejection as set forth for claims 51 and 57 discussed above. Again, Figure 2 clearly shows choline binding protein A truncates, one of which is 460 amino acids in length. Accordingly, while literal support is not required to satisfy 35 U.S.C. §112, first paragraph, literal support for a choline binding protein A

truncate having 460 amino acids is provided in the specification. Thus, for the reason discussed above, claims 52 and 58 do not constitute new matter under 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdrawn the rejection.

Again, as the Examiner's explanation as to why claims 52 and 58 constitute "new matter" were made based on an incorrect interpretation of the claims, if the rejection is maintained, further explanation of the rejection is respectfully requested.

III. The Examiner maintains that claim 60, which recites "up to 398 amino acids," contains "new matter" under 35 U.S.C. §112, first paragraph. This rejection is respectfully traversed.

The Office Action applies the same reasoning for the new matter rejection as set forth for claims 51 and 57 discussed above. Again, Figure 2B clearly shows choline binding protein A truncates, one of which is 398 amino acids in length. While not required to satisfy 35 U.S.C. §112, first paragraph, literal support for a choline binding protein A truncate having 398 amino acids is provided in the specification. Thus, for the reason discussed above, claim 60 does not constitute new matter under 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdrawn the rejection.

Again, as the Examiner's explanation as to why claim 60 constitutes "new matter" were made based on an incorrect interpretation of the claims, if the rejection is maintained, further explanation of the rejection is respectfully requested.

IV. Claims 67, 69 (parts c-e), 70 (parts c-e), 71 (parts a-e), 72 (parts c-e), 74, 75, 81, 87, and 93 were rejected under 35 U.S.C. §112, first paragraph, for "new matter" based on the recitation of the size of the polypeptide. This rejection is respectfully traversed.

The Office Action applies the same reasoning for the new matter rejection as set forth for claims 51 and 57 discussed above. Again, support for "up to 398" amino acids can be found in Figure 2B-2 (claims 67, 71(a), 71(b), and 72(e)); support for "up to 328 amino acids" can be found in Figure 2B-1 (claims 69(c), 69(e), 70(c), 70(e), 71(c), 71(e), 72(c), 72(e) 74, 81, 87, and 93); and, support for "up to 376 amino acids" can be found in the field identifier <121> of SEQ ID NO:7 in the sequence listing (claims 69(d), 70(d), 70(d), 72(d), and 75). While literal support

is not required, literal support for a choline binding protein A truncate having the recited length is found in the specifications and, in light of the reasoning discussed above, claims 67, 69 (parts c-e), 70 (parts c-e), 71 (parts a-e), 72 (parts c-e), 74, 75, 81, 87, and 93 do not contain new matter under 35 U.S.C. §112, first paragraph, and the Examiner is respectfully requested to withdraw the rejection.

Again, as the Examiner's explanation as to why claims 67, 69 (parts c-e), 70 (parts c-e), 71 (parts a-e), 72 (parts c-e), 74, 75, 81, 87, and 93 constitute "new matter" were made based on an incorrect interpretation of the claims, if the rejection is maintained, further explanation of the rejection is respectfully requested.

V. Claim 59 recites "at least 138 consecutive amino acids of SEQ ID NO:24". The Examiner maintains that this claim contains "new matter". Applicants respectfully traverse. First, the specification states that fragments of SEQ ID NO:24 are encompassed by the invention. See, page 6, lines 20-23. Second, Figure 2A discloses various amino acid fragments of choline binding protein A truncates, including a 138 amino acid polypeptide. The specification further provides for "deletions containing less than all of the residues specified in the protein" (see, page 13, lines 5-8). Moreover, the specification provides three species of the claimed genus (i.e., SEQ ID NO:1 which comprises 406 amino acids, SEQ ID NO:3 which comprises 284 amino acids, and SEQ ID NO:24). Accordingly, it is clear that the general concept is disclosed in the specification and contrary to assertions in the Office Action, claim 59 does not constitute new matter.

The Examiner concludes that there is "no general concept disclosed for all polypeptides having the functional properties and size limitations set forth in the claims." However, the recitation of 138 consecutive amino acids of SEQ ID NO:24 is a very predictable structure of the sequences encompassed by claim 59. The Examiner is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000).

The "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" (66 Fed. Reg. 1099, 1106 (2000)) state that genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics, *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993).

The structural limitation recited in claim 59 meets this requirement. The claim recites the identifying structural characteristic that defines the genus of amino acid sequences. Claim 59 recites a fragment that comprises "at least 138 consecutive amino acids of SEQ ID NO:24". This structural limitation is *sufficient to distinguish the claimed nucleotide sequences from other materials and thus sufficiently define the claimed genus*. In addition, as mentioned above, the specification provides three species of the claimed genus (*i.e.*, SEQ ID NO:1 which comprises 406 amino acids, SEQ ID NO:3 which comprises 284 amino acids, and SEQ ID NO:24).

Furthermore, the court in *Lilly* held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus *or* of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." 119 F.3d at 1569, *emphasis added*. The recitation of the structural feature of the presence of a subsequence of SEQ ID NO:24 of a given minimum length is sufficient to satisfy this requirement. Accordingly, this limitation satisfies the written description standard set forth in *Lilly*. The Examiner is respectfully requested to withdraw the rejection of claim 59 for lack of written description under 35 U.S.C. §112, first paragraph.

VI. Claims 60, 61-63, 67-68, 87-89, and 93-94 were rejected as containing "new matter." These claims recite a polypeptide having "at least one to 57 amino acid substitutions". The

Examiner continues to assert that the "generic concept" of a polypeptide having at least one to 57 amino acid substitutions at one to 57 unspecified positions is not disclosed in the specification. The rejection is respectfully traverse.

First, page 13, lines 5-8 of the specification states "one or more amino acid residues may be changed or modified to include variants." Second, page 13, lines 5-8 states that the substitution of the amino acid sequence can comprise replacement of "one or more residues". Third, fifty-seven specific examples of such amino acid changes are provided on pages 13-14 of the specification. Fourth, Figure 2 provides numerous examples of choline binding protein A truncates having various substitutions. Fifth, page 26 describes various amino acid and nucleotide mutations that can be made, including both conservative and non-conservative changes. Sixth, original claims 2-6 and 15-18 recite various truncated N-terminal choline binding proteins and "variants thereof". Therefore, the generic concept of modifying an amino acid sequence at any one of 1 to 57 positions in the recited polypeptide has been disclosed sufficiently for one of skill in the art to understand what is encompassed by the claims. The "new matter" rejection of claims 60 and claims 61-63, 67-68, 87-89, and 93-94 under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Examiner is reminded, that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). As stated above, the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" state that genus may be described by "sufficient description of a representative number of species. . . or by disclosure of relevant, identifying characteristics, *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. Numerous examples of choline binding proteins are provided in Figure 2, and the specification gives the precise location of conserved domains. Furthermore, the recitation of "at least one to 57 amino acid substitutions" is a *very predictable structure* of the sequences encompassed by the claimed invention. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the

species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a polypeptide having at least one to 57 amino acid substitutions to the sequences set forth.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure of at least one to 57 amino acid substitutions to SEQ ID NO: 5, 3, 1, 24, 4, 22, 11, 9, 7, 10, and 23 as recited in the claims is sufficient to satisfy the written description requirement.

Applicants note that the standard for written description set forth in the Office Action is at odds with the "Revised Interim Written Description Guidelines Training Materials" available at www.uspto.gov/web/menu/written.pdf. Example 14 of the "Training Materials" provides a written description assessment for a claim to a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction $A \rightarrow B$. The conclusion in the Training Materials is that the generic claim of Example 14 is sufficiently described under §112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus" and 2) the claim recites a limitation requiring the compound to catalyze the reaction from $A \rightarrow B$, and therefore one of skill in art would recognize that the Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that claims 60, 61-63, 67-68, 87-89, and 93-94 satisfy the written description requirements of §112, first paragraph. Specifically, the claims of the present invention encompass polypeptides having at least one to

57 amino acid substitutions, wherein the polypeptide is immunogenic. As in Example 14, the specification discloses the amino acid sequences that are to have the substitutions, and the claims recite a limitation requiring the polypeptide to have a specific function (*i.e.*, immunogenicity). Accordingly, claims 60, 61-63, 67-68, 87-89, and 93-94 provide the relevant, identifying characteristics that describe the claimed genus, and one of skill in the art would recognize that the inventors were in possession of the claimed invention.

Accordingly, the rejection of claims 60, 61-63, 67-68, 87-89, and 93-94 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn.

VII. Claims 65 and 91 continue to be rejected as containing "new matter" for the recitation of "host preferred amino acid substitutions". Applicants assume the rejection was also intended to be applied to claim 97. Applicants respectfully traverse.

Applicants maintain for the reasons made of record in the Amendment and Response filed December 12, 2002 that the instant specification adequately describes (both explicitly and inherently) to one of skill in the art a polypeptide having "host preferred amino acid substitutions" and the requirements of 35 U.S.C. §112, first paragraph, have been satisfied.

However to expedite prosecution, claims 65, 91, and 97 have been cancelled without prejudice or disclaimer. The rejection of the claims has been obviated.

VIII. Claims 71-72 continue to be rejected for containing "new matter" for the recitation of "retains native tertiary structure." Applicants respectfully traverse.

The Examiner continues to maintain that this is a "new matter" rejection under 35 U.S.C. §112, first paragraph, and states that the specification provides no disclosures of the concept of "native tertiary structure". As made of record in the Amendment and Response filed December 12, 2002, page 7, lines 6-8 of the specification, which contrary to the Examiner's conclusion, provides literal support for this phrase. In addition, the Examiner's attention is drawn to page 6, lines 25-30 of the specification that states:

This invention also provides an isolated polypeptide comprising an amino acid sequence of a N-terminal choline binding protein A truncate ...wherein the polypeptide exhibits its tertiary structure. In one embodiment tertiary structure corresponds to that present in native protein.

In addition, page 7, lines 6-11 of the specification states:

Alternative methods which create a truncated choline binding protein A or fragment thereof, and retain the native tertiary structure (i.e., that of full length choline binding protein A) are contemplated and known to those skilled in the art.

Moreover, original claim 8 of the application recites an N-terminal choline binding protein A truncate "wherein the tertiary structure corresponds to that present in the native protein".

Applicants continue to maintain that in view of the disclosure in the specification and the originally filed claims, claims 71-72 do not constitute "new matter" under 35 U.S.C. § 112, first paragraph.

However, to expedite prosecution claims 71-72 have been amended and no longer recite "retains native tertiary structure". Claims 71-72 now recite "wherein said polypeptide interacts with an antibody, wherein said antibody is also capable of interacting with a full-length CbpA polypeptide". Support for this amendment can be found throughout the specification. See, for example, pages 64 and 65 that outline the development of antibodies that recognize both full-length CbpA proteins and N-terminal truncates of the protein. In fact, Figure 5 and Table 3 (page 63) provide data demonstrating the development of an antibody that recognizes full-length CbpA and an N-terminal fragment. Moreover, the specification provides general support for such antibodies on page 33, lines 29-33 and pages 34 and 35.

Claim 71 and 72 satisfy the requirements of 35 U.S.C. § 112, first paragraph, and the rejection should be withdrawn.

Enablement

I. Claims 69-70 have been rejected under 35 U.S.C. § 112, first paragraph, as being nonenabled. This rejection is respectfully traversed.

Claims 69 and 70 are drawn to an analog or a derivative of a polypeptide set forth in SEQ ID NOS: 1, 3, 4, 5, 7, 9, 10, 11, 22, 23, or 24. In the Final Office Action, the Examiner continues to conclude that "one of ordinary skill would not know what polypeptide to make with respect to claims 69 and 70". The Final Office action maintains that claims 69-70 are not enabled for the reasons of record.

Applicants note that the Office Action mailed August 21, 2002 states "The specification does not appear to define the metes and bounds of an 'analog' or 'derivative'". In the Amendment and Response filed December 12, 2002, Applicants provided the following evidence: 1) page 21, lines 8-11 describes an analog of a polypeptide of the present invention as having a modified N- or C- terminus including, for example, an N-terminal methionine or an N-terminal polyhistidine; 2) a derivative, as explained on page 21, lines 13-19 of the specification, is a polypeptide having one or more chemical moieties attached thereto; and 3) pages 21-26 go on to provide multiple examples of these derivatives and analogs and how they are made. Accordingly, Applicants respectfully submit that the present specification provides ample support for one of skill to make and use analogs and derivatives of the sequences of the invention, and thus, claims 69 and 70 are fully enabled.

MPEP 706.07 states that the final rejection "*should include a rebuttal of any arguments raised in Applicant's reply.*" None appear in the Final Office Action. Applicants continue to maintain that claims 69 and 70 are clearly enabled and the Examiner is respectfully requested to withdraw the rejection of claims 69 and 70 under 35 U.S.C. §112, first paragraph.

If the rejection is maintained, the Examiner is respectfully requested to provide some reason why the disclosure is insufficient, as Applicants contend that the description of analogs and derivatives enables one of skill in the art to make and use the invention.

II. Claims 71-72 have been rejected under 35 U.S.C. §112, first paragraph, as being nonenabled. This rejection is respectfully traversed.

Claims 71-72 were drawn to an isolated polypeptide comprising the amino acid sequence in SEQ ID NOS: 1, 3, 4, 5, 7, 9, 10, 11, 22, 23, or 24, "wherein said polypeptide retains native tertiary structure".

The Examiner continues to maintain that the claim language does not exclude other tertiary structures that the native protein may take under different conditions. However, as made of record in the Amendment and Response filed December 12, 2002 (page 7, lines 1-11), the native tertiary structure of the polypeptide sequences recited in claims 71 and 72, will be the same as the tertiary structure found in the full length choline binding protein. Accordingly, each structure will be compared under identical conditions (i.e., buffers, ligands, etc.) so that a comparison can be made. Applicants maintain for the reasons of record in the Amendment and Response file December 12, 2002 that the term the term "retains native tertiary structure" is fully enabled under 35 U.S.C. §112, first paragraph.

However, to expedite prosecution, claims 71 and 72 have been amended to recite "wherein said polypeptide interacts with an antibody, said antibody is capable of interacting with a full-length CbpA polypeptide." As pages 63-65 and Figure 5 and Table 3 of the specification actually generates an antibody that is capable of interacting with both the full-length CbpA polypeptide and an exemplary polypeptide (i.e. SEQ ID NO:3), sufficient disclosure has been provided to enable the compositions recited in claims 71-72 under 35 U.S.C. §112, first paragraph. The Examiner is respectfully requested to withdraw the rejection of claim 71 and 72.

The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 55 and 82 continue to be rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is respectfully traversed.

The Office Action maintains that claim 55 is confusing as it recites "comprising SEQ ID NO:22" and is dependant on claim 54 that "comprises SEQ ID NO:4". Applicants maintain that the claim is clear. As made of record in the Amendment and Response filed on December 12, 2002, claim 54 recites open language and encompasses a polypeptide having the amino acid sequence set forth in SEQ ID NO:4. Dependant claim 55 is *narrower in scope* as it recites the *longer* amino acid sequence set forth in SEQ ID NO:22. Applicants provide herewith Appendix A that provides a schematic outline of the relationship of the SEQ ID NOS encoding various N-terminal choline-binding proteins. The Appendix has been provided to assist in clarifying the relationship of SEQ ID NO:4 and 22 recited in claim 55. Upon review of Appendix A, it is clear

that, contrary to the conclusions of the Final Office Action, SEQ ID NO:22 comprises SEQ ID NO:4. As such, claim 55 is in proper format and not indefinite. The Examiner is respectfully requested to withdraw the rejection of claim 55 under 35 U.S.C. §112, second paragraph.

Similarly, the rejection of claim 82 was maintained for being confusing as it recites "comprising SEQ ID NO:23 and is dependant on claim 81 which "comprises SEQ ID NO:10." Again, Appendix A illustrates the relationship between the SEQ ID NOS:23 and 10. As clearly illustrated in Appendix, A SEQ ID NO:10 does "comprise" SEQ ID NO:23. Accordingly, Applicants submit that claim 82 is definite and the rejection of claim 82 under 35 U.S.C. §112, second paragraph, should be withdrawn.

Claims 46, 50-52, 54-63, 65-72, 74-78, 81-83, 87-89, 91-94, and 98-98 continued to be rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential elements. This rejection is respectfully traversed.

First, claims 46, 50-52, 54-63, 65-72, 74-78, 81-83, 87-89, 91-94, and 98-98 no longer recite "lectin activity" and now recite "immunogenic". The amendments of claims 46, 50-52, 54-63, 65-72, 74-78, 81-83, 87-89, 91-94, and 98-98 obviates the Examiner's rejection.

However, newly added claims 111-122 have been added and recite that the polypeptide "has lectin activity". The Examiner's concerns regarding indefiniteness are therefore addressed below as they relate to claims 111-122.

To determine the acceptability of claim language under 35 U.S.C. §112, second paragraph, one must determine if one of skill in the art would understand what is claimed. In fact, it is well established that if a claim describes the subject matter so that its scope would be understood by persons in the field of the invention, and the claim distinguishes the claimed subject matter from the prior art, the claim is definite. In the instant case, the claims recite a polypeptide having a specific SEQ ID NO and further state that the polypeptide does not bind choline and has "lectin activity". *It is unclear how one of skill in the art could conclude an element is missing from the claim when the element itself, i.e., the functional language that recites "lectin activity" is explicitly recited in the claim.* Moreover, the specification provides

ample examples of how the "lectin activity" can be measured. See, for example, pages 61 and 62 in which the lectin activity of exemplary polypeptides is determined.

Consequently, one of skill in the art would clearly understand that claims 111-122 of the instant invention encompass polypeptides that *have lectin activity* and moreover, the person of skill in the art would be able to distinguish the claimed subject matter from the prior art. As such, claims 111-122 satisfy the requirements of 35 U.S.C. §112, second paragraph, and the Examiner is respectfully requested to withdraw the rejection.

CONCLUSIONS

The Examiner is respectfully requested to withdraw the rejections and allow claims 46-63, 66-72, 74-78, 80-83, 87-89, 92-95, 98, and 111-122. In any event, the Examiner is respectfully requested to enter the above amendments for purposes of further prosecution. The amendments were not made earlier because the applicant earnestly believes the claims as filed on December 12, 2002 were in conditions for allowance. In addition, the amendments were made pursuant to suggestions made by the Examiner. It is believed that all of the outstanding rejections have been addressed and the claims are ready for allowance. Early notice to this effect is solicited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

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Filed: April 7, 1998

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therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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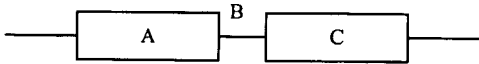
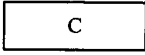
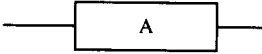
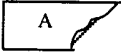
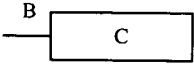
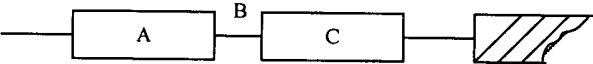
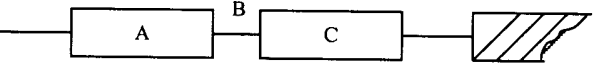

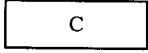
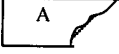
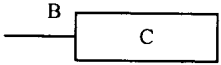
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Marilyn Muñoz

Appendix A

<u>SEQ ID NO</u>	<u>Serotype</u>	<u>Domains</u>	<u>Length</u>
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4	4		106
3	4		284
5	4		109
22	4		121
24	4		428
<hr/>			
7	6		376
9	6		254
10	6		106
11	6		107
23	6		122